Remarks

Claims 1-19 were previously pending in the subject application. By this Amendment, the applicants have amended claims 1, 2 and 6 and have cancelled claims 14-19. Support for the amendments can be found throughout the subject specification and claims as originally filed. No new matter has been added by this Amendment. Accordingly, claims 1-12 are currently before the Examiner. Favorable consideration of the claims now presented is respectfully requested.

The claim amendments have been done to lend greater clarity to the claimed subject matter and to expedite prosecution. The amendment of the claims should not be taken to indicate the applicant's agreement with, or acquiescence to, the rejections of record. Favorable consideration of the claims now presented, in view of the remarks and amendments set forth herein, is earnestly solicited.

Initially, the applicants reaffirm their election of Group I claims, 1-13 for prosecution at this time.

The disclosure has been objected to because of informalities. By this Amendment, the applicants have amended the disclosure of the subject application to comply with the requirement of 37 CFR 1.821 through 1.825. The Office Action further indicates that an initial or substitute computer readable form (CFR) copy of the sequence listing, an initial or substitute paper copy of the sequence listing, as well as an amendment directing entry is needed. However, the applicants submitted a paper copy of the sequence listing as well as an electronic copy and amendment on April 27, 2005 which was accepted as technically good at the Patent Office.

Claims 1-13 have been rejected under 35 U.S.C. §112, first paragraph. The applicants respectfully traverse this ground for rejection because the skilled artisan having the benefit of the applicants' disclosure would be able to readily make and use, without undue experimentation, the modified baculovirus as claimed.

Please note that the claims have been amended herein to lend greater clarity to the claimed subject matter. The applicants respectfully submit that the techniques exemplified in the current application with reference to a vp39 – green fluorescent protein fusion construct could be readily, and without undue experimentation, applied to other heterologous peptides. Specifically, once the

desirability of modifying the capsid is appreciated, the skilled person would have no difficulty in carrying out the invention. The cited prior art shows that the capsid can readily be sequenced; therefore, any desired modification can also be made.

It should be noted that the requirement for some experimentation and/or screening does not necessarily make a claim non-enabled. "Enablement is not precluded by the necessity for some experimentation such as routine screening. . . A considerable amount of experimentation is permissible, if it is merely routine . . ." (emphasis added). *In re Wands,* 8 USPQ 2d 1400, 1404 (Fed. Cir. 1988). In the current case, any experimentation needed to modify other peptides would be routine given the guidance provided in the subject application.

As discussed below, published scientific articles support the applicants' position that those skilled in the art can readily practice the claimed invention. Specifically, the applicants respectfully submit that their own data, as well as the published scientific literature, provide a reasonable expectation that the claimed invention can be used *in* vivo and that peptides other than the vp39 can be used. For example, Oker-Blom *et al.* ("Technique Reviews: Baculovirus display strategies: Emerging tools for eukaryotic libraries and gene delivery," *Briefing and Functional Genomics and Proteomics* 2(3):244-253, 2003) state:

> Recently, a novel molecular biology tool was established by the development of baculovirus surface display, using different strategies for presentation of foreign peptides and proteins on the surface of budded virions. This eukaryotic display system enables presentation of large complex proteins on the surface of baculovirus particles and has thereby become a versatile system in molecular biology. Surface display strategies play an important role, as they may be used to enhance the efficiency and specificity of viral binding and entry to mammalian cells. In addition, baculovirus surface display vectors have been engineered to contain mammalian promoter elements designed for gene delivery both *in vitro* and *in vivo.* Moreover, baculovirus capsid display has recently been developed; this holds promise for intracellular targeting of the viral capsid and subsequent cytosolic delivery of desired protein moieties. (Abstract)

At page 245, the authors go on to state:

> Expression of proteins or peptides on the baculoviral surface, or more recently also on the viral capsid, without comprising replication in insect cells, has shown to be useful for important applications, both *in vivo* and *in vitro.* (citations omitted)

At pages 245-246 the authors further observe that:

In parallel with their use for surface display purposes, baculoviruses were found to enter certain mammalian cell lines efficiently, offering unique opportunities in gene delivery. Modification of viral surface structures by display techniques has enabled the use of baculovirus for enhanced targeting to mammalian cells *in vitro* ... molecules displayed on the baculovirus capsid should escape through the cytoplasm into the nucleus of transduced mammalian cells. Ideally, capsid display should thus enable transfer of functional molecules into the cytoplasm and/or the nucleus of the target cells.

Baculoviruses can accommodate large DNA insertions and grow to high titres, making them satisfactory for the generation of display libraries representing a variety of complex proteins, such as cell surface receptors, viral glycoproteins, ion channels or enzyme complexes, in a stable and functional form. In addition, the regulatory genes evolved solely in insect cells are transciptionally silent in mammalian cells, making the virus safe, with low or no pathogenic potential. Together, these features make the baculoviruses attractive as eukaryotic tools for functional genomics and proteomics and thereby potentially valuable in both basic research and applied biomedical applications such as gene therapy. (citations omitted)

Kukkonen *et al.* (cited in the outstanding Office Action) state at page 856:

Baculoviruses are able to transduce a wide range of mammalian cells *in vitro*. We and others have recently shown that baculovirus-mediated gene transfer works also *in vivo*. (citations omitted)

Kukkonen *et al.* go on to note that:

Our results are consistent with a recent electron microscopic study of baculovirus entry and transport steps in Pk1 epithelial pig kidney cells and confirm also that baculovirus capsid is transported together with the viral genome into the nucleus of the cells compatible with baculovirus-mediated gene transfer.

• • •

As the entry of baculovirus into mammalian cells and the release of the viral capsid into the cell cytoplasm seem to be general phenomena, the concept of baculovirus-mediated therapy may further be extended with the possibility of using the baculovirus capsid as a shuttle for the transport of therapeutic proteins into cells analogous to protein transduction schemes.

In addition to these published scientific articles, the inventors have data showing that p24 can also be used as a fusion partner in a baculovirus capsid display system.

Please note that it is well established in the patent law that the mere possibility of an inoperable embodiment does not render a claim non-enabled. "It is not necessary that every permutation within a generally operable invention be effective in order for an inventor to obtain a generic claim, provided that the effect is sufficiently demonstrated to characterize a generic invention." Capon *v.* Eshhar, 418 F.3d 1349, 1359 (Fed. Cir. 2005). Furthermore, it is well settled that patent applicants are not required to disclose every species encompassed by their claims, even in an unpredictable art. In re Angstadt, 537 F.2d 498, 502-03, 190 U.S.P.Q (BNA) 214, 218 (CCPA 1976). In the current case, the applicants are not aware of any inoperable embodiments and have no reason to believe that any exist. Thus, in the absence of any specific reason to doubt the ability of one skilled in the art to practice the subject invention, the applicants respectfully submit that the invention, as claimed, is fully enabled.

In summary, there is no reason to doubt that the applicants' teachings will apply to the modification of baculoviruses as currently claimed and the applicants' claims should not be limited only to the specific exemplification provided in the applicants' specification. Accordingly, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §112.

Claims 1-7, 10 and 11 have been rejected under 35 U.S.C. §102(b) as being anticipated by Liu *et al.* (Acta Virolgica, 2000, 44:157-161). The applicants specifically traverse this ground for rejection because Liu *et al.* do not disclose or suggest a baculovirus having a modified capsid that displays one or more heterologous peptides.

The applicants' claims require that the baculovirus capsid display one or more heterologous peptides. Heterologous peptides are, by definition, not present in the naturally occurring capsid. Liu *et al.* does not disclose any such peptides.

It is basic premise of patent law that, in order to anticipate, a single prior art reference must disclose within its four corners, each and every element of the claimed invention. In *Lindemann v. American Hoist and Derrick Co.*, 221 USPQ 481 (Fed. Cir. 1984), the court stated:

> Anticipation requires the presence in a single prior art reference, disclosure of each and every element of the claimed invention, arranged as in the claim. *Connell v. Sears Roebuck and Co.*, 722 F.2d 1542, 220 USPQ 193 (Fed. Cir. 1983); *SSIH Equip. S.A. v. USITC*, 718 F.2d 365, 216 USPQ 678 (Fed. Cir. 1983). In deciding the issue of anticipation, the [examiner] must identify the elements of the claims, determine their meaning in light of the specification and prosecution history, and identify corresponding elements disclosed in the allegedly anticipating reference. *SSIH, supra*; *Kalman [v. Kimberly-Clarke*, 713 F.2d 760, 218 USPQ 781 (Fed. Cir. 1983)] (emphasis added). 221 USPQ at 485.

Please note that the claims have been amended herein to clarify that the baculovirus has been modified such that a heterologous peptide is displayed on the capsid. Liu *et al.* do not disclose (or even suggest) any such modified baculovirus. Accordingly, because the cited reference does not disclose each and every element of the claimed invention, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §102(b) based on the Liu *et al.* reference.

Claims 6, 7, 9, 10 and 12 have been rejected under 35 U.S.C. §102(b) as being anticipated by Van Loo *et al.* (Journal of Virology, 2001, 75(2):961-970). The applicants specifically traverse this ground for rejection because Loo *et al.* do not disclose or suggest a baculovirus having a modified capsid that displays one or more heterologous peptides.

As noted above, anticipation requires that a single prior art reference disclose, within its four corners, each and every element of the claimed invention.

Please note that the claims have been amended herein to clarify that the baculovirus has been modified such that a heterologous peptide is displayed on the capsid. Van Loo *et al.* do not disclose (or even suggest) any such modified baculovirus. Accordingly, because the cited reference does not disclose each and every element of the claimed invention, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §102(b) based on the Van Loo *et al.* reference.

In view of the foregoing remarks, the applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

The applicants also invites the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephone interview would expedite the prosecution of the subject application to completion.

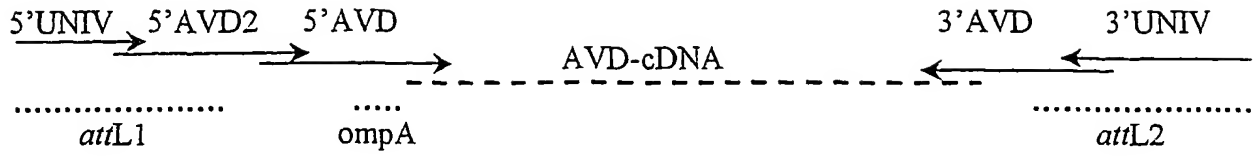
Respectfully submitted,

David R. Saliwanchik
Patent Attorney
Registration No. 31,794
Phone: 352-375-8100
Fax No.: 352-372-5800
Address: P.O. Box 142950
Gainesville, FL 32614-2950

DRS/la

Attachments: Copy of Oker-Blom *et al.* reference
Replacement Drawing Figure 5
Annotated Drawing of Figure 5 (showing changes)

A



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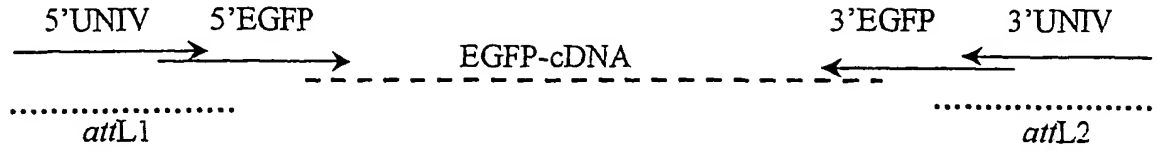

C 5'UNIV: 5'-*CAAATAATGA TTTTATTTTG ACTGATAGTG ACCTGTTCGT TGCAACAAAT TGATAAGCAA TGCTTTTTTA TAATGCCAAC TTTGT*-3' (SEQ ID NO: 11)

3'UNIV: 5'-*CAAATAATGA TTTTATTTTG ACTGATAGTG ACCTGTTCGT TGCAACAAAT TGATAAGCAA TGCTTTCTTA TAATGCCAAC*-3' (SEQ ID NO:12)

5'AVD: 5'-CGC TCT GGC GCT TGC CTT CGC CGC CGT TAC GGC CTC TGG TGT TGC CTC GGC TCA GAC CGT GGC CAG AAA GTG CTC GCT GAC-3' (SEQ ID NO:13)

5'AVD2: 5'-*GCT TTT TTA TAA TGC CAA CTT TGT ACA AAA AAG CAG GCT* ATG AAC AAA CCC TCC AAA TTC GCT CTG GCG CTT GCC TTC G-3' (SEQ ID NO:14)

3'AVD: 5'-*TGC TTT CTT ATA ATG CCA ACT TTG TAC AAG AAA GCT GGG TAT* TAC TCC TTC TGT GTG CGC AGG-3' (SEQ ID NO:15)

5'EGFP: *TTA TAA TGC CAA CTT TGT ACA AAA AAG CAG GCT* ATG GTG AGC AAG GGC GAG (SEQ ID NO:16)

3'EGFP: 5'-*TGC TTT CTT ATA ATG CCA ACT TTG TAC AAG AAA GCT GGG* TTT ACT TGT ACA GCT CGT C-3' (SEQ ID NO:17)

Figure 5